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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,632	09/08/2003	Alex Chenchik	SBIO/0002	6082

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EXAMINER	
STEELE, AMBER D	

ART UNIT	PAPER NUMBER
1639	

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09/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/658,632	CHENCHIK, ALEX	
	Examiner	Art Unit	
	Amber D. Steele	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-28* is/are pending in the application.

4a) Of the above claim(s) *19,20 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,21-24 and 26-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 January 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/15/05;8/25/05;2/20/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Please note: the examiner of record for the present application has changed. However, the Technology Center (TC1600) and Art Unit (AU1639) remain the same.

Status of the Claims

2. Claims 1-23 were originally filed on September 8, 2003.

The amendment to the claims received on October 24, 2007 amended claim 17, canceled claims 1-16, and added new claims 24-28.

The amendment to the claims received on February 20, 2008 canceled claim 17, amended claims 18-27, and added new claim 29.

The amendment to the claims received on June 6, 2008 canceled claim 29.

Claims 18-28 are currently pending.

Claims 18, 21-24, and 26-28 are currently under consideration.

Election/Restrictions

3. Applicant's election of Group I (claims 18-28) in the reply filed on June 6, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

4. Applicant's election of 1000 effector sequences as the species of number and siRNA as the species of effector sequence in the reply filed on June 6, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

5. Claims 19-20 and 25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on June 6, 2008.

Priority

6. The priority date for the present application is the filing date of September 8, 2003.

Information Disclosure Statement

7. The information disclosure statements (IDS) submitted on September 15, 2005; August 25, 2005; and February 20, 2004 are being considered by the examiner in part.

Citation #5 requires additional information (e.g. date, page numbers, volume, source, etc.). Citation #13 requires a publication date. For citation numbers B1 and B3, only the abstracts (i.e. English translation) were considered. Regarding the International search report, only the references provided separately on the IDS and copies provided where appropriate were considered.

Drawings

8. The drawings are objected to because Figures 9, 10, and 12 contain sequences without proper SEQ ID NOs: (please note: for a complete response, a new sequence listing, CRF, and letter stating the CRF and sequence listing are the same may be required). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as

"amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

9. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 18, 21-24, and 26-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent

Applications under the 35 USC 112, first paragraph "Written Description" requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a **written description** rejection.

Independent claims 26 and 27 are drawn to a method for making a packaged viral effector library comprising (a) synthesizing a set of at least 100 different effector nucleic acid sequences on a surface of a microarray wherein each nucleic acid sequence has a specific sequence and is synthesized in a specific location of the surface, (b) detaching the set of nucleic acid sequences from the microarray, (c) amplifying the detached set of nucleic acid sequences from the microarray via PCR, and (d) cloning the defined set of nucleic acid sequences into viral expression vectors to produce a library of effector constructs and variations thereof. The invention as claimed encompasses all known nucleic acid sequences and viral expression vectors and all potential nucleic acid sequences and viral expression vectors since virtually any nucleic acid sequence can be inserted into a viral expression vector. The elected species of siRNA and the requirement for 100 or 1,000 heterogenous siRNA further exacerbates the lack of written description because the specification does not disclose a single siRNA. The claimed invention does not include any structural information regarding the nucleic acid except that the nucleic acid encodes a cDNA, siRNA, peptide, or protein (i.e. elected species of siRNA, functional limitation). In addition, the claimed invention does not include any structural information regarding the viral vector except that the vectors can be lentiviral (see claims 21-22).

The specification teaches lentiviruses including HIV, visan-maedi, CAE, EIAV, FIV, BIV, and SIV (please refer to paragraph 40). In addition, the specification also teaches utilizing the pL-reporter lentiviral backbone, pLSLP which is similar to other known retroviral vectors

(please refer to paragraphs 78-79; Figures 3, 9). Furthermore, the specification is silent regarding a single, specific species of nucleic acid which encodes cDNA, siRNA, peptides, or proteins much less at least 100 or 1,000 heterogenous nucleic acid sequences. In particular, the specification refers to a genus of siRNAs which are 19 or 27 bp in length (see paragraph 80 for example). Furthermore, the specification does not teach if any of the generic siRNA discussed actually function as siRNA. Therefore, one skilled in the relevant art would not reasonably conclude that the Applicants had possession of the invention as claimed since the structural limitations are not included in the claims.

See Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was *in possession of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See page 1116.).

With the exception of the specific vectors disclosed in the specification, the skilled artisan cannot envision the method of claims 26 or 27, particularly wherein the product produced via the method as claimed requires at least 100 or 1,000 heterogenous siRNAs. For example Li et al., 2007, Predicting siRNA efficiency, Cell. Mol. Life Sci., 64: 1785-1792 teach that the efficiency of siRNA is dependent on the siRNA sequence, siRNA secondary structure, mRNA (i.e. target) secondary structure, etc. and that off-target effects can prevent the use of siRNA as treatments, etc. (see page 1787-1788). Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See

Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class wherein the specification provided only the bovine sequence.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 18, 21-24, and 26-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beraud et al. WO 2004/108897 (effective filing date of June 2, 2003) and Adessi et al., 2000, Solid Phase DNA Amplification: characterization of primer attachment and amplification mechanisms, Nucleic Acids Research, 28(20): e87, 8 pages.

For present claims 26-28, Beraud et al. teach methods comprising solid phase synthesis of DNA encoding siRNA, detaching the DNA from the solid phase, amplification via PCR, cloning into viral vectors, and packaging (please refer to the entire specification particularly paragraphs 5-10, 47-52, 57-58, 71-72, 78-79, 86-87, 92-95; Figures).

For present claim 18, Beraud et al. teach 10^6, 10^8, 10^9, or 2.7×10^{11} siRNA (please refer to the entire specification particularly paragraph 78 and 87).

For present claims 21-22, Beraud et al. teach retroviral and lentiviral expression vectors (please refer to the entire specification particularly paragraphs 71-72, 92-95).

For present claims 23-24, Beraud et al. teach siRNA (please refer to the entire specification particularly paragraphs 6).

However, while Bernaud et al. teach solid-phase synthesis on beads and oligonucleotides on microarrays, Bernard et al. doees not specifically teach solid-phase synthesis on microarrays.

For present claims 26-27, Adessi et al. teach solid phase DNA amplification (i.e. combined synthesis and amplification steps; please refer to the entire reference particularly the abstract; Figures 1-2).

The claims would have been obvious because the substitution of one known element (i.e. bead based solid phase synthesis or bead as taught by Beraud et al.) for another (i.e. microarray based solid phase synthesis or glass slide as taught by Adessi et al.) would have yielded predictable results (i.e. solid-phase synthesis of oligonucleotides) to one of ordinary skill in the art at the time of the invention. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

14. Claims 18, 21-24, and 26-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caplan et al. US 2003/0149113 published August 7, 2003; Fosnaugh et al. U.S. 2003/0148507 published August 7, 2003; and Barone et al. U.S. Patent 7,026,114 (filing date of November 30, 1995 and effective filing date of September 13, 1995).

For present claims 26-28, Caplan et al. teach methods comprising solid phase synthesis of DNA encoding siRNA, cloning into viral vectors, and packaging (please refer to the entire specification particularly 23, 32, 47, 95-96, 179-186).

For present claims 21-22, Caplan et al. teach retroviral and lentiviral vectors (please refer to the entire specification particularly paragraphs 23, 184).

For present claims 23-24, Caplan et al. teach siRNA (please refer to the entire specification particularly paragraph 95).

However, Caplan et al. does not teach a specific number of siRNA.

For present claims 18 and 26-27, Fosnaugh et al. teach an siRNA library comprising 4^{19} members, solid support synthesis of siRNA, cleaving of siRNA from the supports, and cloning into vectors inclduign retroviral vectors (please refer to the entire specification particularly Figures 1 and 9; paragraphs 13-14, 25-26, 83, 91-94, 135-145, 153, 158-171).

However, while both Caplan et al. and Fosnaugh et al. teach solid-phase synthesis utilizing beads, solid-phase synthesis utilizing a microarray is not taught.

For present claims 26-27, Barone et al. teach microarray based solid phase synthesis comprising synthesis of polymers including nucleic acids on supports including slides, cleavage of polymers form the support, and amplification via PCR (please refer to the entire specification particularly Figure 2; columns 2, 4, 10-11, 13, 20).

The claims would have been obvious because the substitution of one known element (i.e. bead based solid phase synthesis or bead as taught by Caplan et al. or Fosnaugh et al.; siRNA population with an unknown size taught by Caplan et al.) for another (i.e. microarray based solid phase synthesis or glass slide as taught by Barone et al.; siRNA library of a specific size as taught by Fosnaugh et al.) would have yielded predictable results (i.e. solid-phase synthesis of oligonucleotides; potentially more diverse library; library of definitive size) to one of ordinary

skill in the art at the time of the invention. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/
Patent Examiner, Art Unit 1639

September 22, 2008